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EXAMINER
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POPA, ILEANA

ART UNIT	PAPER NUMBER
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1633

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08/17/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/580,037	<b>Applicant(s)</b> POULIQUEN ET AL.	
	<b>Examiner</b> ILEANA POPA	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-19 and 21-39 is/are pending in the application.
- 4a) Of the above claim(s) 24-27,30-34,38 and 39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-19,21-23,28,29 and 35-37 is/are rejected.
- 7) ☒ Claim(s) 7 and 28 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. The applicant argues that, since Huille et al. do not anticipate the presently amended claim 1, the instant claims share a "special technical feature" not found in the prior art and the restriction requirement should be withdrawn. This is not found persuasive because the presently amended claim 1 is rendered *prima facie* obvious over Huille et al., in view of the prior art (please see the obviousness-type rejection below). For this reason, the restriction requirement is maintained.

Claims 2 and 20 have been cancelled. Claims 24-27 and 30-34 have been withdrawn. The new claims 38 and 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to the nonelected inventions of Groups II and III, there being no allowable generic or linking claim. Claims 1, 3, 4, 7-10, 16-18, and 21 have been amended. Claims 36-39 are new.

Claims 1, 3-19, 21-23, 28, 29, and 35-37 are under examination.

2. Acknowledgement is made of applicant's submission of an English language translation of foreign priority document.

All rejections pertaining to claims 2 and 20 are moot because the applicant cancelled the claims in the reply filed on 05/18/2010.

The objection to claim 17 is withdrawn in response to the amendments filed on 05/18/2010.

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The following rejections are withdrawn in response to the amendments filed on 05/18/2010:

The rejection of claims 1, 4-12, 16-19, 21-23, and 28 under 35 U.S.C. 112, second paragraph, as being indefinite;

The rejection of claims 1-23, 28 and 29 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21, 28-32 and 40 of U.S. Patent No. 6,630,171;

The provisional rejection of claims 1-23, 28 and 29 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims , over claims 1-10, 15, 17-24 and 26 of the copending Application No. 10/516,733;

The rejection of claims 1, 6, 7, 16, 18, 21 and 28 under 35 U.S.C. 102(b) as being anticipated by Huille et al. (WO 00/30618);

The rejection of claims 1, 5-8, 12-16, 18, 20-23 and 28 under 35 U.S.C. 103(a) as being unpatentable over Huille et al., in view of Edwards et al. (Arch. Dermatol., 1990, 126: 1029-1032, Abstract);

The rejection of claims 1-4, 6, 7, 16, 18, 21, 28, and 29 under 35 U.S.C. 103(a) as being unpatentable over of Huille et al., in view of each Eliaz et al. (J. Biomed. Mater. Res., 2000, 50: 388-396), Regalado et al. (Macromolecules, 1999, 32: 8580-8588, Applicant's IDS) and Akiyoshi et al. (Macromolecules, 1997. 30: 857-861).

### ***Claim Listing***

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3. It is noted that, in the Office action mailed on 02/18/2010, claims 12-15 were rejoined. However, the claims are identified as “withdrawn”. Correction to identify the claims as “original” is required.

### ***Claim Objections***

4. Claim 7 is objected to because of the following informalities: the claim recites a rate which “varies from 1 to mol%”. Appropriate correction to indicate the upper limit is required.

5. Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, claim 1 recites that the active principle (AP) is interferon. Claim 28, which directly depends from claim 1, recites the broad genus of AP and thus fails to further limit claim 1 which is drawn to one specific species of AP.

### ***Response to Arguments***

#### ***Double Patenting***

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined

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application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 3-19, 21-23, 28, 29, and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 12-22, 25, 26, 28, 29, 35 and 36 of copending Application No. 10/580,035. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to the same polymer formulation for prolonged delivery of therapeutic agents. Although the instant claims recite interferon and not interleukin, one of skill in the art would have found it obvious to replace the interleukin with interferon.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1, 3-19, 21-23, 28, 29, and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-

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20, 25 and 27 of copending Application No. 11/878,947, over claims 1-16, 21, 22, 24-26, 28 and 29 of copending Application No. 10/580,023, over claims 1-3, 5-16, 19, 21, 22, 24-26, 28, and 29, of the copending Application No. 11/808,456, over claims 1-10, 16, 18-24 of the U.S. Patent 7,683,024 (filed as Application No. 10/516,733), and over claims 1-4, 6-11, 15, 16, 18-21, 26-30, 38 and 39 of the copending Application No. 12/003,095. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the applications claims are drawn to the same polymer formulation for prolonged delivery of therapeutic agents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The applicant argues that the cited applications 10/580,035, 11/878,947, 10/580,023, 11/808, 456, 11/658, 803, and 12/003,095 cannot be used to reject the claims because they have a later priority date. This is not found persuasive because the applications above are not used as art to reject the claims under 35 U.S.C. 102 or 35 U.S.C. 103(a). The applicant is reminded that double patenting rejections can be made over the claims of later filed applications. Thus, it is proper to make and maintain the double patenting rejections, unless they are the only rejections remaining in at least one of the applications (see MPEP 822.01[R-3]). In the instant case, the double patenting rejections are not the only remaining rejections and thus, they are maintained.

### ***New Rejections***

**Double Patenting**

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1, 3-19, 21-23, 28, 29, and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21, 28-32 and 40 of U.S. Patent No. 6,630,171, in view of each Regalado et al. (Macromolecules, 1999, 32: 8580-8588, of record), Dupuis et al. (U.S. Patent No. 6,607,714), and Bromberg et al. (U.S. Patent No. 5,939,485). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the patent claims are drawn to the same polymer formulation for prolonged delivery of interferon. The patent claims do not recite gel-forming properties. However, modifying the patent claims to obtain injectable solutions capable of *in situ* gelling is

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suggested by the prior art. Controlled and prolonged drug release via injectable formulations capable of gelling *in vivo* was routine in the prior art. The prior art also suggests that the polymer of the '171 patent is capable of forming a gel *in vivo* in the presence of physiological proteins. For example, the prior art teaches that incorporation of HG into hydrophilic polymers results in amphiphilic polymers which are capable of sol to gel transition depending on the amphiphilic polymer concentration (see Regalado et al., p. 8580, column 1; p. 8587, column 2). Dupuis et al. teach that amphiphilic polymer solutions are capable of forming gels in the presence of serum proteins such as albumin (Examples 4 and 5). Bromberg et al. teach the necessity of using responsive polymers capable of forming a gel in the presence of an environmental stimulus (such as a stimulus present *in vivo*), wherein adjusting the concentration of the responsive polymer gives the desired sol to gel transition (Abstract; column 2, lines 17, 18, and 63-65 ; column 6, lines 43-56; column 11, lines 20-40, claims 5, 18, and 32). Based on these teachings as a whole, one of skill in would have known that the amphiphilic polymer of the '171 patent is capable of sol to gel transition. One of skill in the art would also have reasonably expected that the polymer at concentrations promoting the sol to gel transition would be able to form a gel when injected *in vivo*, because albumin is present in blood and in the interstitial fluid. Therefore, one of skill in the art would have been motivated to vary the polymer concentration such as to determine the proper concentration needed to obtain a liquid formulation capable to form a gel in the presence of albumin (claim 3). It is noted that by doing such, one of skill in the art

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would have obtained a formulation capable of forming a gel deposit *in vivo* in the presence of physiological proteins.

Thus, the instant claims are obvious variants of the patent claims.

11. Claims 1, 3-19, 21-23, 28, 29, and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, and 12-22 of copending Application No. 11/658,803 because the instant claims and the application claims are drawn to the same polymer formulation for prolonged delivery of interferon, wherein the polymer is capable of forming a gel (i.e., a depot) upon administration *in vivo* (i.e., in the presence of albumin). Since the polymer solution recited in the application claims is liquid before administration and forms a gel upon administration, it must have the polymer concentration and the viscosity recited in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 1, 3-19, 21-23, 28, 29, and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-25 of copending Application No. 10/558,617. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the application claims are drawn to the same polymer formulation for prolonged delivery of interferon, wherein the polymer is capable of forming a gel upon

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administration *in vivo* (i.e., in the presence of albumin). Since the polymer solution recited in the application claims is liquid before administration and forms a gel upon administration, it must have the polymer concentration and the viscosity recited in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1, 3-19, 21-23, 28, 29, and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 7,659,365, in view of each Regalado et al. (Macromolecules, 1999, 32: 8580-8588, of record), Dupuis et al. (U.S. Patent No. 6,607,714), and Bromberg et al. (U.S. Patent No. 5,939,485). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the patent claims are drawn to the same polymer formulation for prolonged delivery of interferon. The patent claims do not recite gel-forming properties. However, modifying the patent claims to obtain injectable solutions capable of *in situ* gelling is suggested by the prior art. Controlled and prolonged drug release via injectable formulations capable of gelling *in vivo* was routine in the prior art. The prior art also suggests that the patent polymer is capable of forming a gel *in vivo* in the presence of physiological proteins. For example, the prior art teaches that incorporation of HG into hydrophilic polymers results in amphiphilic polymers which are capable of sol to gel transition depending on the amphiphilic polymer concentration (see Regalado et al., p. 8580, column 1; p. 8587,

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column 2). Dupuis et al. teach that amphiphilic polymer solutions are capable of forming gels in the presence of serum proteins such as albumin (Examples 4 and 5). Bromberg et al. teach the necessity of using responsive polymers capable of forming a gel in the presence of an environmental stimulus (such as a stimulus present *in vivo*), wherein adjusting the concentration of the responsive polymer gives the desired sol to gel transition (Abstract; column 2, lines 17, 18, and 63-65 ; column 6, lines 43-56; column 11, lines 20-40, claims 5, 18, and 32). Based on these teachings as a whole, one of skill in the art would have known that the amphiphilic patent polymer is capable of sol to gel transition. One of skill in the art would also have reasonably expected that the polymer at concentrations promoting the sol to gel transition would be able to form a gel when injected *in vivo*, because albumin is present in blood and in the interstitial fluid. Therefore, one of skill in the art would have been motivated to vary the polymer concentration such as to determine the proper concentration needed to obtain a liquid formulation capable to form a gel in the presence of albumin (claim 3). It is noted that by doing such, one of skill in the art would have obtained a formulation capable of forming a gel deposit *in vivo* in the presence of physiological proteins.

Thus, the instant claims and the patent claims are obvious variants.

14. Claims 1, 3-19, 21-23, 28, 29, and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 7,678,882. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the patent claims are

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drawn to the same polymer formulation for prolonged delivery of interferon, wherein the polymer formulation is capable of forming a gel upon administration *in vivo* (i.e., in the presence of albumin). Since the polymer solution recited in the patent claims is liquid before administration and forms a gel upon administration, it must have the polymer concentration and the viscosity recited in the instant claims.

Thus, the instant claims and the patent claims are obvious variants.

### ***Claim Rejections - 35 USC § 103***

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. Claims 1, 3-8, 12-16, 18, 21, 22, 28, 29, 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. (WO 00/30618, of record), in view of each Regalado et al. (Macromolecules, 1999, 32: 8580-8588, of record), Dupuis et al. (U.S. Patent No. 6,607,714), and Bromberg et al. (U.S. Patent No. 5,939,485).

The English language translation of WO 00/30618 is US Patent 6,630,171. The passages cited below which indicate the teachings of the '618 publication are based on its English translation (i.e., the '171 patent).

Huille et al. teach a liquid, low viscosity formulation suitable for parenteral injection and prolonged release of interferon, wherein the formulation is liquid in physiological medium and wherein the formulation comprises an aqueous colloidal

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suspension of submicronic particles in water and interferon(IFN) non-covalently-associated with the particles. The particles are made of homopolymers of  $\alpha$ -aspartate or  $\alpha$ -glutamate or of aspartate/glutamate copolymers (i.e., water-soluble polymers) carrying hydrophobic groups (HG), the HG could be cholesterol, the molar grafting rate is between 3 and 70%, the polymers contain up to 200 amino acids (i.e., n+m is 200) and the molecular weight of the polymer could be 20,000 g/mol; the polymers could have a structure as set forth in formula I (claims 1, 6, 7, 16, 18, 21 and 28) (Abstract; column 3, lines 25-65; column 4, lines 6-65; column 5, lines 45-61; column 9, lines 35-41; Example 1). Huille et al. also teach further attaching polyethylenimine (PEI) (claims 36 and 37) (column 7, lines 30-36).

Although Huille et al. teach homopolymers of  $\alpha$ -aspartate or  $\alpha$ -glutamate, they do not specifically teach that the amino acid precursors are L-aspartate or L-glutamate (claim 12-14). However, it would have been obvious to one of skill in the art to use such to achieve the predictable result of obtaining a polymer suitable for the controlled release of IFN. With respect to claim 15, Huille et al. teach their polymers as being either random or block polymers (column 7, lines 58-60).

Huille et al. do not specifically teach their HG being attached to the terminal ends of the polymer (i.e., formula IV recited in claim 8). However, it is noted that there is no evidence on the record that attaching the HG at the terminal ends of the polymer results in an unexpected property. The arrangement (i.e., where the HG is attached to the polymer) is not significant if it does not provide a novel feature. Moreover, it would have been obvious to one of skill in the art to vary the arrangement, with the purpose to

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achieve the optimum results. Absent evidence to the contrary, it is generally not inventive to discover the optimal arrangement of a prior art composition, such can be identified by routine experimentation.

Although Huille et al. teach a degree of association for insulin > 90% (Example 7), they do not specifically teach the same degree for IFN (claim 22). However, one of skill in the art would have reasonably expected to obtain the same high degree of association when using IFN.

Huille et al. do not specifically teach a polymer concentration which allows the formation of a gel deposit *in vivo* in the presence of at least one physiological protein (claim 1, 28, 29, and 35). However, controlled and prolonged drug release via injectable formulations capable of gelling *in vivo* was routine in the prior art. The prior art also suggests that the polymer of Huille et al. is capable of gel *in vivo* in the presence of physiological proteins. For example, the prior art teaches that incorporation of HG into hydrophilic polymers results in amphiphilic polymers which are capable of sol to gel transition depending on the amphiphilic polymer concentration (see Regalado et al., p. 8580, column 1; p. 8587, column 2). Dupuis et al. teach that amphiphilic polymer solutions are capable of forming gels in the presence of serum proteins such as albumin (Examples 4 and 5). Bromberg et al. teach the necessity of using responsive polymers capable of forming a gel in the presence of an environmental stimulus (such as a stimulus present *in vivo*), wherein adjusting the concentration of the responsive polymer gives the desired sol to gel transition (Abstract; column 2, lines 17, 18, and 63-65 ; column 6, lines 43-56; column 11, lines 20-40, claims 5, 18, and 32). Based on these

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teachings as a whole, one of skill in the art would have known that the amphiphilic polymer of Huille et al. is capable of forming a sol to gel transition. One of skill in the art would also have reasonably expected that the polymer at concentrations promoting the sol to gel transition would be able to form a gel when injected *in vivo*, because albumin is present in blood and in the interstitial fluid. Therefore, one of skill in the art would have been motivated to vary the polymer concentration such as to determine the proper concentration needed to obtain a liquid formulation capable to form a gel in the presence of albumin (claim 3). It is noted that by doing such, one of skill in the art would have obtained a formulation capable of forming a gel deposit *in vivo* in the presence of physiological proteins, wherein the formulation comprises a concentration of polymer as recited in claims 1 and 4 and wherein the viscosity is up to 5 Pas at 20°C (claim 5).

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

17. Claims 1, 3-8, 12-16, 18, 21-23, 28, 29, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. taken with Regalado et al., Dupuis et al., and Bromberg et al., in further view of Edwards et al. (Arch. Dermatol., 1990, 126: 1029-1032, Abstract, of record).

The teachings of Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. are applied as above for claims 1, 3-8, 12-16, 18, 21, 22, 28, 29, and 35-37. Although Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. teach IFN, they do not

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specifically teach IFN- $\alpha$  (claim 23). Edwards et al. teach treatment of basal cell carcinoma via administration of controlled-release formulation comprising IFN- $\alpha$  (Abstract). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the formulation of Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. by substituting their IFN with IFN- $\alpha$  to achieve the predictable result of obtaining a formulation suitable for the controlled-release of IFN- $\alpha$ .

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

18. Claims 1, 3-8, 12-18, 21, 22, 28, and 29, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. taken with each Regalado et al., Dupuis et al., and Bromberg et al., in further view of both Kim et al. (U.S. Patent No. 5,869,703, of record) and Seo et al. (U.S. Patent No. 7,311,901, of record).

The teachings of Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. are applied as above for claims 1, 3-8, 12-16, 18, 21, 22, 28, 29, and 35-37. Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. do not teach tocopherol (claim 17). However, using tocopherol to obtain biocompatible amphiphilic polymers is taught by the prior art (see Kim et al., column 1, lines 9-18, column 2, lines 20-55; Seo et al., Abstract, column 4, lines 10-30). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the polymer of Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. by substituting their cholesterol with tocopherol to achieve the predictable result of obtaining a polymer suitable for prolonged IFN delivery.

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With respect to claim 19, it would have been obvious to one of skill in the art to vary the polymer concentration such as to determine the proper concentration needed to obtain a liquid formulation capable to form a gel *in vivo*.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

19. Claims 1, 3-16, 18, 21, 22, 28, 29, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. taken with each Regalado et al., Dupuis et al., and Bromberg et al., in further view of Conover et al. (Anti-Cancer drug Design, 1999, 14: 499-506, of record).

The teachings of Huille et al., Eliaz et al., Regalado et al., Dupuis et al., and Bromberg et al. are applied as above for claims 1, 3-8, 12-16, 18, 21, 22, 28, 29, and 35-37. Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. do not teach coupling their cholesterol via an amino acid spacer (claims 9-11). However amino acid spacers (including alanine and phenylalanine) were routinely used in the prior art to create polymers suitable for drug delivery (see Conover et al., Abstract, p. 502, Tables I and II, p. 504, column 1). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the polymer of Huille et al., Regalado et al., Dupuis et al., and Bromberg et al. by using an amino acid spacer to couple the cholesterol to their polymer to achieve the predictable result of obtaining a polymer suitable for sustained release of TNF.

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Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

20. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Ileana Popa/  
Primary Examiner, Art Unit 1633

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